DEPARTMENT OF THE NAVY
NAVAL MEDICAL COMMAND
WASHINGTON, D.C. 20372-5120

IN REPLY REFER TO

NAVMEDCOMINST 6570.1
MEDCOM-313
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NAVMEDCOM INSTRUCTION 6570.1

From: Commander, Naval Medical Command

Subj: ANTINEOPLASTIC DRUG GUIDELINES

Ref: (a) Occupational Safety and Health Administration (OSHA) Instruction PUB 8-1.1 dtd January 29, 1986

Encl: (1) Guidelines for the Preparation of Antineoplastic Drugs
(2) Guidelines for the Administration of Antineoplastic Drugs
(3) Guidelines for Preparation and Application of Topical Nitrogen Mustard
(4) Guidelines for the Prevention and Handling of Antineoplastic Drug Spills
(5) Guidelines for the Collection and Disposal of Antineoplastic Drugs
(6) Medical Surveillance of Occupational Exposure to Antineoplastic Drugs

1. Purpose. To provide policy and guidelines for Naval Medical Command (NAVMEDCOM) activities using antineoplastic drugs, and to ensure the implementation of reference (a).

2. Background. Antineoplastic drugs are used for treating malignant diseases. These drugs are usually diluted or dissolved before administration to patients. The handling and administration of these drugs may chronically expose medical personnel to cytotoxic agents. Concern has been raised on the potential teratogenic or carcinogenic effects of these drugs. Some of these drugs also have the potential of causing irritation to the eyes, skin, and mucous membranes. Exposure to antineoplastic drugs generally occurs during preparation and administration. Exposure may occur by skin contact, inhalation of the aerosols created during the handling of syringes, accidental self-inoculation, and contact with the excreta from patients treated with these drugs.

3. Action. Any command unable to comply with all requirements of this instruction shall not use antineoplastic drugs without written approval from COMNAVMEDCOM. All activities where antineoplastic drugs are used are responsible for implementing the guidelines established in enclosures (1) through (6). Commanding officers or officers in charge shall:

a. Appoint an antineoplastic drug officer to establish, manage, and monitor the antineoplastic drugs control program at the command.

b. Document the implementation of reference (a) and this instruction to include:

(1) A registry (file) requirement, listing all antineoplastic drugs used or stored in the facility. Maintainance of this registry will be by the occupational medicine division of the hospital or clinic and will be made available to employees. (Reference (a), section IVH.)

(2) A training program for personnel who may be required to work with antineoplastic drugs to ensure proper workplace practices. (Reference (a), section IVH.)

(3) A surveillance program to medically evaluate all personnel who are exposed, or potentially exposed, to antineoplastic drugs. (Reference (a), section IVF.)

(4) An emergency plan to deal with spillages and accidents involving antineoplastic drugs. (Reference (a), section IVE.)

(5) Disposal procedures for wastes containing antineoplastic drugs, ensuring that they are in accordance with enclosure (5) and local, State, and Federal regulations. (Reference (a), section IVD.)

(6) A log to identify personnel who are required to work or come in contact with antineoplastic drugs. This log shall be kept by the occupational health officer. (Reference (a), section IVF.)

(7) The use of approved equipment that has been properly vented, and use of adequate workplace practices in preparing and administering antineoplastics.

(8) Adequate storage and transportation of antineoplastics. (Reference (a), section IVG.)

c. Provide adequate security to prevent accidental antineoplastic drug contamination of hospital staff and visitors; conduct inspections to ensure compliance with reference (a); and review inspection findings at least annually to verify acceptable conformance to this instruction.

4. Forms. OPNAV 5100/15, Medical Surveillance Questionnaire, is available from local Navy Publication and Printing Service Office.

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GUIDELINES FOR THE PREPARATION OF ANTINEOPLASTIC DRUGS

1. Assignment of Personnel. Train personnel concerning the proper use and limitations of the specific safety cabinets in use. See paragraph 3b of the basic instruction. Assign only personnel trained in the proper preparation of antineoplastic drugs to such tasks, in accordance with manufacturer's recommendations.

2. Protective Apparel. Instruct personnel preparing antineoplastic drugs to wear disposable surgical gloves -- double latex gloves preferred -- and a solid front disposable gown with long sleeves and elastic or knit cuffs. Gowns may be washable, but a disposable type is preferred. Remove gloves and protective garments when overly contaminated. Discard gloves after each use. Do not wear gowns outside preparation areas.

3. Preparation Area. Conduct preparation of antineoplastic drugs in a specific room designed for that purpose whenever possible. If a room is not available, set aside a section of a room for such a purpose. Allow only authorized personnel in such areas. Properly label areas to warn of potential hazards. Place a warning label on the hood.

4. Preparation Procedures. Perform all procedures involving the preparation of antineoplastic drugs in accordance with reference (a), and preferably in a Class II (vertical laminar flow) biological safety cabinet. Specify certain safety cabinets for the sole purpose of preparing antineoplastic drugs. When workload does not justify purchase of a biological safety cabinet, goggles and a respirator are mandatory.

a. Check proper functioning of the safety cabinet before use. Place all supplies and equipment needed for the preparation of the drugs on the safety cabinet before starting formulation.

b. Cover the working surface of the safety cabinet with a plastic backed absorbent paper to reduce dispersion of aerosols, control spills, and facilitate clean-up. Change the paper as required, and at the end of each work shift.

c. Conduct all handling and mixing of drugs on the work surface of the safety cabinet away from the exhaust ports. Maintain the laminar flow and negative pressure across the face opening of the cabinet by limiting arm movements in and out of the cabinet.

d. Institute a scheduled maintenance program for Class II biological safety to include maintenance of the high efficiency particulate air (HEPA) filters. Verify proper functioning of the

safety cabinets at least semiannually, and after installation, repairs, and relocation. Ventilation measurements shall be made to ensure that manufacturer's design specifications are maintained.

e. Personnel performing maintenance of biological safety cabinets used to prepare antineoplastic drugs, shall be informed of the hazards of such drugs and in the proper handling and disposal of contaminated HEPA filters and any other contaminated parts or materials.

5. Aseptic Techniques. Use aseptic techniques for patient and manipulator safety while preparing the drugs.

a. Wash hands before and after using gloves. Use of gloves is no substitute for hand washing. Gloves should be tucked into the gown's cuff, and changed at least every 30 minutes with continued use or when overly contaminated. (Wrist and arm skin shall not be exposed.)

b. When breaking the top of the glass ampules, wrap the neck of the ampules at the anticipated break point with a sterile alcohol dampened pledget. This will help to maintain sterile conditions, contain aerosol produced, protect fingers from laceration, and avoid flying pieces of glass.

c. Use negative pressure whenever drugs to be reconstituted are being prepared. This will prevent pressure build-up within the vial, and reduce the possibility of spraying or spillage when a needle is withdrawn from the vial septum.

d. Carefully wrap a sterile alcohol dampened cotton pledget around the needle and vial top during withdrawal from the vial septum, and when ejecting air bubbles from filled syringe. Avoid self inoculation.

e. Wipe clean of drug contamination the external surfaces of syringes, I.V. bottles, and other glassware.

f. Recap used needles and syringes, and dispose of them intact to prevent aerosol generation created by clipping needles. For disposal, place used needles and syringes in leak proof containers that are puncture resistant.

g. After drug preparation is completed, wipe down the interior of the safety cabinet and other working surfaces with 70 percent alcohol, using gauze pads.

h. Properly label syringes and intravenous (I.V.) bottles containing antineoplastic drugs before they are placed in sealable plastic bags (e.g., ziplock) to be taken from the

preparation area. A second label warning of the drug hazards, proper methods of disposal, and any other required information should be affixed to the outside of a ziplock plastic bag or other protective cover and titled appropriately (e.g., "CANCER CHEMOTHERAPY, DISPOSE OF PROPERLY").

6. Emergency Precautions

a. During emergencies and circumstances when a Class II biological safety cabinet is not available, provide personnel preparing antineoplastic drugs with the personal protective equipment described above, a National Institute of Occupational Safety and Health (NIOSH) approved dust and mist approved respirator, and a face shield or eye goggles.

b. Provide an eye wash station, capable of flushing the eye for at least 15 minutes, located next to the preparation area. Provide medical evaluation after the flushing of the eyes. Use soap and water to thoroughly wash any other affected area.

GUIDELINES FOR THE ADMINISTRATION OF ANTINEOPLASTIC DRUGS

1. Kit for Administration. A kit may be superfluous in many situations; however, one may be prepared to facilitate the administration of antineoplastic drugs, if deemed appropriate. Suggested items to be included in the kit are:

a. Written procedures for the administration of antineoplastic drugs and kit disposal.

b. Disposable tray with plastic backed absorbent paper.

c. Two sets of disposable latex surgical gloves. Thin polyvinyl chlorine (PVC) gloves should not be used for handling these drugs.

d. Assorted sizes of gauze and alcohol wipes.

e. Plastic jars and vials with screw-on tops of assorted sizes for the disposal of used ampules and excess drug solutions. Sealable plastic bags may be used.

f. A plastic bag (minimum 4 mils) large enough for disposal of all waste material (to include gowns, etc.) at the end of the administration of the drugs.

g. A surgical mask or NIOSH approved dust/mist respirator is required.

h. Disposable eye protection equipment, one set.

2. Precautions for Personnel. Allow only personnel trained in proper use, disposal, and emergency procedures for the handling of antineoplastic drugs to administer such drugs. Familiarize the personnel administering antineoplastic drugs with the specific drugs to be handled, and manufacturer's recommendations for the drug's proper use.

a. Wear protective gowns, disposable gloves, surgical mask, and eye protection; and dispose of them appropriately after use.

b. Wash hands before and after the administration of antineoplastic drugs, and after the administration and disposal of contaminated equipment.

3. Administration Procedures

a. Handling Injections

(1) Removal of air from I.V. tubing may be accomplished by back priming the air into the I.V. bag.

(2) Cap contaminated needles and syringes and dispose of them intact to prevent aerosol generation created by clipping needles.

(3) Infusion sets and pumps should have luer-lock fittings and should be watched for leakage during use. Collect any leakage in a plastic lined absorbent pad. If infusion lines need bleeding, bleed them into a sealable container with a gauze inside.

b. Handling of Oral Dosage Forms

(1) Many tablets, particularly the alkylating agents, have either an outer compression coating with the drug in an inner core, or they are film coated. There is no handling risk if the coatings are not broken down. A small number of tablets are made from compressed powders. Many of these tablets are extremely friable and should be counted in a specified counting tray under a vertical flow hood with an OSHA approved biological safety cabinet. Capsules, whether hard or soft gelatin, are free from risk unless they are opened or have broken or leaked.

(2) Do not open or crush tablets and capsules. Personnel dispensing tablets and capsules should not touch them at any stage. Use forceps or wear double surgical latex gloves.

(3) Use a counting tray restricted for antineoplastic drug use, and clean it with alcohol swabs after each prescription order is filled.

(4) Formulate any pediatric suspension compound using the biological safety cabinet. The precautions and equipment necessary to protect the formulator are described in enclosure (1).

(5) In the event of spillage, take the precautions described under the handling and spillage of injections in enclosure (4).

GUIDELINES FOR PREPARATION AND APPLICATION OF TOPICAL NITROGEN MUSTARD

1. Protective Apparel. Use protective apparel when preparing and applying nitrogen mustard. Dispose of protective apparel and application equipment in the chemotherapy waste receptacle for incineration. This protective apparel will include:

a. Long-sleeved disposable protective garments.

b. Double surgical latex gloves.

c. Glasses (safety goggles and/or prescription lens glasses).

d. Disposable surgical masks.

2. Preparation. Nitrogen mustard solution for topical use must be prepared just prior to application to ensure potency. Prepare nitrogen mustard for topical application in the pharmacy. The pharmacy will coordinate with the ward for preparation of the solution prior to application.

3. Isolation Area. Place patients receiving topical nitrogen mustard in a ward or clinic isolation room, and adjust venting for that room to ensure that negative pressure exists.

4. Application

a. Apply topical nitrogen mustard solutions during the day shift to ensure the availability of staff trained to prepare and apply it. This also ensures that staff is available to educate patients and family members on safe preparation and application of topical nitrogen mustard. Patients or family members may apply nitrogen mustard on an inpatient basis as part of their training for discharge, or when they have been applying it routinely on an outpatient basis.

b. Apply topical nitrogen mustard solution by paint brush or other acceptable means with downward strokes only.

5. Emergency Procedures

a. If eye contact with nitrogen mustard should occur, copiously irrigate the eyes with water for 15 minutes to be followed by prompt opthalmologic examination.

b. If skin contact occurs, irrigate the affected part immediately with copious amounts of water for at least 15 minutes, followed by 10 percent sodium thiosulphate solution.

6. Clean Up Procedures. At the end of the treatment, soak the paint brush, tray, and excess solution for 45 minutes in a solution of equal parts of 5 percent sodium bicarbonate and 5 percent sodium thiosulfate solution. After soaking, clean the paint brush and tray with soap or detergent and water for future use. Soak all reusable equipment used in compounding and application in a solution of equal parts of 5 percent sodium bicarbonate and 5 percent sodium thiosulfate. This soaking neutralizes the nitrogen mustard and its metabolites. The equipment is to be soaked for 45 minutes, after which it may be safely cleaned.

GUIDELINES FOR THE PREVENTION AND HANDLING OF ANTINEOPLASTIC DRUG SPILLS

1. Assignment of Personnel. Allow only personnel trained in the proper cleanup of antineoplastic drugs spills and in the use of personal protective equipment to perform such duties. Limit the personnel conducting drug spill cleanups, manage them separately from the regular housekeeping staff; and instruct them to keep spills separate.

2. Prevention and Readiness

a. Storage and Transportation

(1) Store antineoplastic drug containers in medicine cabinets separate from other medications. Store containers on specific shelves that have barriers to prevent vials or bottles from falling to the floor. Provide storage areas that are easily accessible.

(2) Do not temporarily store antineoplastic drugs on counters or carts outside the preparation and storage areas. Transport them directly from the preparation and storage areas to the administration area, and do not leave them unattended.

b. Assemble a Spill Kit. Keep inactivators readily available. Neutralize antineoplastic drugs, for which chemical inactivators exist, by using inactivating solutions before cleanup. Special spill kits are available commercially. As a minimum, spill kits should contain the following items:

(1) Personnel protective equipment consisting of 2 pairs of surgical latex gloves; 2 sets of protective clothing (Tyvek suits are ideal) to include footwear covers; 2 dust/mist disposable respirators; and disposable eye protection equipment.

(2) Absorbent materials such as packages of 1:1 mixtures of vermiculite and J.T. Baker Solusorb, absorbing pillows, and sheets of absorbing materials.

(3) Chemical inactivators to neutralize antineoplastic drugs, before cleanup.

(4) Four plastic waste disposal bags of heavy duty (at least 4 mils polyethylene) construction, sealable, and labeled on their contents and proper disposal. Double bagging is recommended before transportation for incineration.

3. Spills inside Biological Safety Cabinets; Control by

a. Operating the ventilation system during cleanup. If antineoplastic drugs are spilled through the intake vents and the HEPA filters are heavily contaminated, discontinue use of the unit until completion of decontamination, following the manufacturer's recommendations.

b. For liquid spills, clean up with absorbent material and use absorbent material to dike intake vents to prevent further contamination of the cabinet. Do not place diking material on the vents at the edge of the working surface. Continue cleanup by absorbing drugs with absorbent material and properly dispose of waste materials.

c. For dust contamination, wipe with wet absorbent gauze or disposable towels and properly dispose of waste materials.

d. Clean spills thoroughly with sterile water, and finally with 70 percent alcohol.

e. If removal of the face cabinet becomes necessary, a dust/mist respirator and eye protection will be required.

4. Spills in Other Areas, Control by

a. Limiting area of the spill as much as feasible by covering liquid agents with absorbent materials, and powders with moistened cloths or disposable towels.

b. Treating all contaminated surfaces with detergent solutions, and cleaning with water after spill is controlled.

c. Isolating the area and contacting the spill team.

d. Having the spill team wear gloves, respirators (if required), eye protection, and protective clothing to clean up the area and dispose of all noncleanable items.

5. Report of Spills. Report records of spills and injuries received during the cleanup of spills to the antineoplastic drug officer. The antineoplastic drug officer will ensure that the spill kits are refurbished after each use. Inspect kits at least annually.

GUIDELINES FOR THE COLLECTION AND DISPOSAL OF ANTINEOPLASTIC DRUGS

1. Training. Provide documented training to all personnel coming in contact with antineoplastic drug waste materials to include: hazards of the drugs, proper use of personal protective equipment, and proper collection and disposal of waste materials.

2. Collection and Disposal System

a. Develop a system for the collection and disposal of antineoplastic drugs waste for each facility that uses these drugs. Separate this system from other medical facility's waste disposal systems.

b. Prepare and post standard operating procedures for the routine and emergency collection and disposal of antineoplastic drugs in areas of antineoplastic drugs preparation and disposal.

3. Handling Techniques

a. Use surgical latex gloves to collect and dispose of antineoplastic waste containers, and instruct personnel in procedures governing spills and leaks, in case of container breakage.

b. Use separate covered waste containers marked "ANTINEOPLASTIC DRUG WASTE ONLY".

c. Use waste containers lined with properly labeled plastic bags (4 mils polyethylene) which are emptied at least daily. Seal bags before transportation.

d. Place glass fragments, needles, and syringes in puncture resistant containers before placing them in plastic bags.

e. Consider human waste from patients with antineoplastic drugs as hazardous waste, such as vomitus, urine, feces, and other body fluids. Unmetabolized drugs or mutagenic metabolites may constitute a potential hazard and personnel that come in contact with this waste are to avoid skin contact and minimize aerosol generation during disposal. Use personal protective equipment during disposal of human waste. This waste may be discharged into the regular sanitary sewer.

4. Disposal. Conduct disposal of all antineoplastic drugs and all drug contaminated items in accordance with local, State, and Federal regulations. When permitted, conduct disposal by:

a. Inactivating large amounts chemically before disposal, if possible, and dispose in a properly labeled plastic bag.

b. Incineration at 2000° - 2200° F. (1102.08°C.-1214.08°C.)

c. Burial in an approved toxic waste landfill.

d. Contracting with a hazardous waste disposal company.

MEDICAL SURVEILLANCE OF OCCUPATIONAL EXPOSURE TO ANTINEOPLASTIC DRUGS

1. Background

a. Antineoplastic drugs form a heterogeneous group of chemicals, many of which are known mutagens, carcinogens, or teratogens in animals. A few are carcinogens in humans treated with high-dose parenteral administrations. Some are vesicants which can damage the unprotected skin or eyes.

b. Medical surveillance is undertaken as a precautionary measure. A theoretical health risk is posed to occupationally-exposed hospital personnel. There has been no firm evidence of disease caused by chemotherapeutic agents in hospital personnel.

c. Personnel who are routinely and repetitively exposed to chemotherapeutic agents in the course of admixture, compounding, and administration are to be included in a medical surveillance program. Minimize the number of designated personnel working with these agents.

2. Preplacement Physicals. Provide designated personnel with preplacement physicals which will serve as a basis for subsequent comparison. Identify their health records, "Occupational Exposure to Chemotherapeutic Agents." The preplacement record should include:

a. Medical history, including family history of neoplasia, smoking, reproductive history, immunosuppressive drugs, cytotoxic drugs, radiation therapy, nuclear pharmaceuticals, and cancer.

b. Occupational history, including periods of previous employment, locations, type of work, and known work hazards. For work involving potential exposure to antineoplastic agents, record type of work, location, and identification and approximate handling frequency for antineoplastic drugs. The occupational history shall be recorded on Medical Surveillance Questionnaire, OPNAV 5100/15. (Reference OPNAVINST 5100.23B.)

c. Physical examinations with attention to eyes and skin.

d. Laboratory screening, including complete blood count with differential, and urinalysis with microscopic exam. The differential examination is to be performed regardless of the white blood cell count. Additional laboratory screening may be required by the examining physician, depending upon known physiologic effects of specific chemotherapeutic agents to which personnel are routinely and repetitively exposed.

3. Periodic Medical Surveillance. Provide yearly medical surveillance as follows.

a. Update of the medical and occupational histories.

b. Physical and laboratory examination comparable to the pre-placement physical examination.

c. All the above data should be reviewed by the occupational health medical officer, and entered as part of the employee's medical record.

4. Acute Exposures. Employees who have an acute exposure to an antineoplastic agent should have a repeat physical examination and should be followed every 6 months with an exam and laboratory work for a period of 2 years regardless of their subsequent lack of exposure. At that time, if that employee is asymptomatic and the laboratory results have been stable, the employee should revert back to the schedule noted (1) above. Procedures for acute exposures follows.

a. The occupational health service is to offer treatment to personnel acutely or accidentally exposed to antineoplastic drugs; and direct treatment to the particular drug, mode of exposure, and clinical presentation. The nature and frequency of followup shall be at the discretion of the occupational health physician.

b. The hospital safety department is to document acute exposure episodes, and the occupational health physician is to examine the employee.

c. Report all such incidents to appropriate safety personnel.